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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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MORGAN LEWIS & BOCKIUS LLP
1111 PENNSYLVANIA AVENUE NW
WASHINGTON, DC 20004

EXAMINER	
WOITACH, JOSEPH T	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 06/02/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/939,709	BARON ET AL.	
	Examiner	Art Unit	
	Joseph T. Woitach	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18,23,24 and 31-47* is/are pending in the application.

4a) Of the above claim(s) *1-18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23,24 and 31-47* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This application filed August 28, 2001 claims benefit to provisional application 60/228,450, filed August 29, 2000.

Applicants' amendment filed March 11, 2004, has been received and entered. Claims 19-22 and 25-30 have been cancelled. Claims 34, 35 and 38 have been amended. Claims 45-47 have been added. Claims 1-18, 23, 24 and 31-47 are pending.

Election/Restriction

Applicant's election with traverse of Group IV, in Paper No. 16 was acknowledged. The election of species was withdrawn. Newly added claims 45-47 are drawn to the elected invention. Applicants have not provided any new arguments in traverse of the restriction requirement, therefore the requirement is still deemed proper.

Claims 1-18, 23, 24 and 31-47 are pending. Claims 1-18 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made without traverse in Paper No. 16. Claims 23, 24, 31-47, drawn to a method of identifying genes which are modulated by ΔFosB are currently under examination.

Claim Objections

Claim 38 objected to because the claim ends with a semicolon is withdrawn.

The amendment to the claim to insert a period instead of a semicolon has obviated the objection.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 33 rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention is withdrawn.

Applicants argue that all of the cell lines except Ros 17/2.8 are publicly available as evidenced by their availability in the ATCC catalog. With respect to the cell line Ros 17/2.8, Applicants argue that its wide use in the art is evidence of its routine use and public availability. See Applicants' amendment, pages 7-8. Applicants' arguments have been fully considered and found persuasive.

The information from the ATCC catalog has been reviewed by the Examiner supports Applicants' assertion. Because these cell lines were publicly available at the time of the claimed invention, a deposit requirement is not necessary. Similarly, the evidence provided supports that the Ros 17/2.8 cell line is known and routinely used in the art as asserted by Applicants. Because of the wide public use and variety of sources, a deposit requirement of Ros 17/2.8 is not required (see MPEP 2404 and 37 CFR 1.802).

In light of the public availability of the claimed cell lines, the rejection is withdrawn.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 34, 35 and newly added claims 46 and 47 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Initially, the amendment to claim 38 has obviated the basis of each of the specific rejections. With respect to claims 40 and 42, Applicants' arguments have been considered and found persuasive (see Applicants amendment, bridging pages 8-9). Examiner agrees that the claims are not indefinite, and would be clear to one of ordinary skill in the art.

Claims 34, 35, 46 and 47 are vague, unclear and incomplete in how the lysates and extracts are used in the method set forth in claims 23 and 45. Claims 34 and 35 have been amended to indicate the method "further comprises", however it is unclear when this method step is performed or how it is related to assaying differences in gene expression. More generally, for each 34, 35, 46 and 47 it is unclear how providing a lysate or extract is specifically associated with determining which genes are differentially expressed. More clearly detailing the method steps in determining how genes that are differentially expressed are determined using either the lysate or extract would address the basis of the rejection.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 23, 24, 31, 32, 36-45 are rejected under 35 U.S.C. 102(b) as being anticipated by Nestler *et al.* (IDS reference).

Applicants summarize the basis of the claimed invention and argue that Nestler *et al.* do not teach the claimed method. Specifically Applicants argue that only the expression of ΔfosB is demonstrated in Nestler *et al.*, and the general plans for using the disclosed transgenic mice is not a disclosure of the claimed method. See Applicants' amendment, page 9, section A.

Applicants do not contest the fact that the transgenic animals represent a method of inducing ΔFosB in a cell which is step (a) of independent claims 23 and 45. Applicants' arguments rely on the fact that Nestler *et al.* do not provide evidence that step (b) was reduced to practice or results of practicing step (b). Examiner acknowledges that the only specific results presented by Nestler *et al.* after step (a) is the analysis of the induction and expression of ΔFosB, however Nestler *et al.* teach that ΔFosB targets, including expression of gene targets and identification of novel proteins, has been successfully reduced to practice (page 16, first column, first full paragraph). It is recognized that the results of these experiments are not provided, but clearly step (b) of the claimed method has been reduced to practice by Nestler *et al.* Moreover, Nestler *et al.* specifically teach that the analysis of ΔFosB affect was successfully accomplished

using DNA array technology, a technique specifically claimed (claim 24 and 41) (page 16, first column, end of first full paragraph). In addition, the evidence provided in figure 4 does provide analysis after the induction of ΔFosB of the various isoforms ranging form 35-37kDa. Further, the instant claims are broad and do not indicate any restriction on the gene to be detected after the induction of ΔFosB. Thus, even the analysis of ΔFosB by Nestler *et al.* anticipates step (b) of the claimed method because one were interested in the absolute affect of the induction process on ΔFosB as evidenced in the characterization of the model by Nestler *et al.* Applicants' arguments are not found persuasive because Nestler *et al.* provide a model system for the induction of ΔFosB in cells and provide the teaching that the model has been successfully used in conjunction of DNA array technology to assay the affects of ΔFosB expression. The limitations encompassed by the instantly claimed method are anticipated by the teaching of Nestler *et al.*

As summarized in the previous office action, Nestler *et al.* teach that ΔFosB targets and its role of in neural plasticity *in vitro* and *in vivo* in animal models (page 12, bridging first and second columns). Nestler *et al.* teach that ΔFosB is known to be induced by cocaine, amphetamine nicotine, opiates, antidepressants, and antipsychotic (see Table 1). Because Nestler *et al.* practices the methods in animals all the cells of the animal are affected including those set forth in claim 32. Further, Nestler *et al.* teach to generate transgenic ΔFosB mice and use said mice in analyzing the affect of ΔFosB (pages 1-15, section 4 and 5). Nestler *et al.* isolate RNA and do Northern blot analysis to determine the affects of ΔFosB expression in a transgenic animal in various parts of the brains and in various organs and tissues (figure 4). Nestler *et al.* teach that they have used DNA array technology with early success (page 16, end

of section 5, citing results of citation 7-Chen *et al.* IDS reference). Nestler *et al.* teach that ΔFosB is a transcription factor whose expression is an early response to stimuli (page 10, abstract and introduction section) and that the materials and methods disclosed are used to detect altered expression of specific target genes (page 16, end of section 6).

Finally, it is noted that Applicants have not provided any arguments in traverse of Examiner's analysis for the use of a DNA array. Specifically, this methodology is considered to be high throughput because it multiple samples are assayed at one time. Furthermore, it is noted that in general simply setting forth that a known method is done by using automated methods is not considered patentable. See *In re Venner*, 262 F.2d 91, 95, 120 USPQ 193, 194 (CCPA 1958) where it was held that a process that was previously done manually and the only difference with the prior art and the claimed invention is that the process is automated and accomplishes the same result is not sufficient to distinguish it over the prior art. See MPEP 2144.iii.

Claims 23, 31, 32 and 37-40 rejected under 35 U.S.C. 102(b) as being anticipated by Agamemnon *et al.* (J Cell Biol 122:685-701, 1993) is withdrawn.

Applicants summarize the basis of the claimed invention and argue that Agamemnon *et al.* do not teach the claimed method. Specifically Applicants argue that only the expression of c-fos is demonstrated in Agamemnon *et al.* which is different from ΔFosB. See Applicants' amendment, bridging pages 9-10, section B.

Examiner notes that a fosB-LTR construct was used and the resulting transgenic animal analyzed by Agamemnon *et al.* (see Table 1, third construct). However, there were no phenotypic affects on bone pathology and further characterization focused on the affects of c-fos.

The rejection is withdrawn because Agamemnon *et al.* does not teach each limitation of the instantly claimed method.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 23, 31, 33, 34, 35, 45, 46 and 47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nestler *et al.* and Agamemnon *et al.*

Nestler *et al.* is summarized above. Briefly, Nestler *et al.* teach that ΔFosB is known to be induced by cocaine, amphetamine nicotine, opiates, antidepressants, and antipsychotic in animals (see Table 1). Further, Nestler *et al.* teach to generate transgenic ΔFosB mice and use said mice in analyzing the affect of ΔFosB (pages 1-15, section 4 and 5), and practices the methods in animals all the cells of the animal are affected. Nestler *et al.* isolate RNA and do Northern blot analysis to determine the affects of ΔFosB expression in a transgenic animal in various parts of the brains and in various organs and tissues (figure 4). Nestler *et al.* teach that they have used DNA array technology with early success (page 16, end of section 5, citing

results of citation 7-Chen *et al.* IDS reference). Thus, Nestler *et al.* teach that ΔFosB is an inducible transcription factor whose expression is an early response to stimuli (page 10, abstract and introduction section) and that the materials and methods disclosed are used to detect altered expression of specific target genes (page 16, end of section 6). Nestler *et al.* teach and provide the necessary guidance that anticipates claims 23, 24, 31, 32, 36-39, 41-44. Agamemnon *et al.* teach a transgenic mouse model where the fosB is provided as a transgene under the control LTR promoter, and that it is expressed in a variety of tissues. The expression of the transgene results in the expression of the exogenous fosB transcripts (see figure 2, panel B and summarized in Table I). Further, Agamemnon *et al.* teach the isolation of cell lines (starting on bottom of page 691 and Table III), and the characterization of the affect of the transgene on specific gene expression *in vivo* and *in vitro* in the isolated cell lines (see Figures 5 and 8 for example) and specifically teaches to use the Ros 17/2.8 cell line (claim 33)(page 695, bottom of second column). The combined teaching of Nestler *et al.* and Agamemnon *et al.* provide clear guidance for the expression of fos transcriptional factors and for the analysis of the consequences of this expression by a variety of methodology known in the art. Further, Nestler *et al.* provides specific materials and guidance for the analysis ΔFosB for its role in the brain in neuropsychiatric disorders. Agamemnon *et al.* teach a different transgenic mouse expressing fosB under a different promoter providing a second model system to study the affect in varied expression patterns and tissue distribution. Nestler *et al.* specifically discloses using DNA arrays and provides guidance for doing protein Western blots and RNA northern blots to study changes in expression. Such methodology is well known in the art, but neither Nestler *et al.* and Agamemnon *et al.* specifically disclose that the cell lystates or nuclear extracts were made in the

analysis of RNA or protein from whole cell or nuclear fractions. However, providing cell lysates and nuclear extracts are required to practice the methodology outlined by Nestler *et al.* and Agamemnon *et al.* Further, the other methods specifically recited in the claim 44 that are not taught by Nestler *et al.* nor Agamemnon *et al.* such as RT PCR, RNAase protection and subtractive hybridization are well known methods in the art routinely used in the analysis of gene expression. Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to use cell lysates and nuclear extracts in the analysis of changes in expression. One having ordinary skill in the art would have been motivated to use whole cell lysates to analyze changes in total protein in methods like SDS-PAGE or Western blots or in the isolation of RNA, and to use nuclear extracts for the analysis of specific changes in nuclear factors, in particular because fosB is part of a large family of transcriptional factors whose presence in various levels provides the complex regulation of early gene expression in response to a variety of stimuli in a variety of tissue and cell types. There would have been a reasonable expectation of success given the level of skill in the art and the routine nature of the methodology claimed that one could analyze RNA by any of the methods known and used in the art at the time of filing.

Thus, the claimed invention as a whole was clearly *prima facie* obvious.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (571) 272-0739.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached at (571) 272-0734.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group analyst Dianiece Jacobs whose telephone number is (571) 272-0532.

Joseph T. Woitach

Joe Woitach
AU1632